Peste des Petits Ruminants

Disease Monograph Series - 02

Virus | Morbillivirus | *Paramyxoviridae* | Goats | Sheep

IDRC | Bartay

This monograph forms part of a series of disease monographs commissioned by the International Development Research Centre over the period Nov 2015 to April 2016 to inform funding priorities for the Livestock Vaccine Innovation Fund (LVIF). The LVIF is a seven-and-a-half year, CA$57 million partnership between the Bill & Melinda Gates Foundation, Global Affairs Canada and Canada's International Development Research Centre. It focuses on those animal diseases posing the greatest risk to poor livestock keepers in Sub-Saharan Africa, South and Southeast Asia, targeting transboundary diseases to achieve lasting regional impact.

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Acronyms

AU	African Union
AU-IBAR	African Union Inter-African Bureau for Animal Resources
AU-PANVAC	African Union – Pan African Vaccine Centre
BMGF	Bill & Melinda Gates Foundation
C-ELISA	Competitive Enzyme-linked immunosorbent assay.
CFT	Complement fixation test
CI	Confidence Interval
CPV	Capripox virus
CVO	Chief Veterinary Officer
DG	Director General
DIVA	Differentiation between infected and vaccinated animals
DoI	Duration of immunity
DVS	Director Veterinary Services
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
IAEA	International Atomic Energy Agency of the United Nations
icELISA	Imunocapture enzyme-linked immunosorbent assay
ILRI	International Livestock Research Institute

IM	Intramuscular
KALRO	Kenya Agricultural and Livestock Research Organization
KEVEVAPI	Kenya veterinary vaccine production institute
LAMP	Loop-mediated isothermal amplification
LAT	Latex agglutination test
LIPS	Luciferase Immunoprecipitation System
NGO	Non-governmental organization
OIE	World Animal Health Organization
PCR	Polymerase chain reaction
Pfu	plaque forming units
PPR	Peste des petits ruminants
PPRV	Peste des petits ruminants virus
QC	Quality control
QRT-PCT	Quantitate reverse transcription polymerase chain reaction
REC	Regional Economic Community
RPV	Rinderpest virus
RT-PCR	Reverse transcription polymerase chain reaction
SADC	Southern African Development Community
SAT	Slide agglutination test
SC	Subcutaneous
SHF	Small holder farmer
TPP	Target Product Profile

Executive Summary

The disease, etiology, epidemiology and impact

Peste des petits ruminants (PPR) is an acute contagious viral disease of sheep and goats. PPR is caused by a Morbillivirus in the family Paramyxoviridae. The virus has a lipid envelope which contains the fusion (F) and haemagglutinin (H) glycoproteins. All virus strains belong to a single serotype, but the different strains have been grouped in 4 distinct lineages.Goats and sheep are the primary hosts for PPRV with few reports in camels. Cattle, buffalo and pigs develop subclinical infection but are not capable of excreting the virus and are not considered epidemiologically relevant. Young animals are most severely affected, and goats more than sheep. In its peracute form animals are found dead. Clinical signs include fever, depression, loss of appetite, and clear nasal discharge. This nasal discharge becomes mucopurulent and can result in a profuse catarrhal exudate which crusts and occludes the nostrils causing respiratory distress. There is congestion of the conjunctiva, and sometimes profuse catarrhal conjunctivitis. Ulcers are formed on the lower gums, dental pad, hard palate, cheeks and tongue. Necrotic stomatitis is common. Severe diarrhoea develops in some animals. Pregnant animals may abort. Morbidity rate in susceptible populations can reach 90–100%. Mortality rates vary among susceptible animals but can reach 50–100% in more severe instances. The disease is transmitted though aerosol or animal excretions. PPR threatens more than 1.7 billion of sheep and goats, as well as the livelihoods, and food security of more than 330 million people. It is estimated that the direct annual losses due to PPR are between USD 1.2 and 1.7 billion. The estimated current expenditure on PPR vaccination ranges between USD 270 and 380 million. The annual impact of PPR may be valued at between USD 1.45 and 2.1 billion per year.

Incidence / Prevalence

Since its first identification in the early 1940s in Côte d'Ivoire, PPR has steadily expanded. It occurs now in most African countries from North Africa to Tanzania. Also in large parts of Central Asia, South Asia and East Asia. It is present in the Arabian Peninsula, and nearly all Middle Eastern countries. Of the focus countries, Myanmar and South Africa have OIE official freedom status. The disease is not present in Southern Africa, but there have been a couple of outbreaks in Zambia and there are fears of the disease spreading from the neighbouring countries.

Diagnostics

The OIE Terrestrial Manual described methods for the agent identification include virus isolation, immunocapture ELISA, counter immunoelectrophoresis and agar gel immunodiffusion. Polymerase chain reaction (PCR) may also be used. The serological tests routinely used are the virus neutralization test and the competitive ELISA. A field test, a lateral flow device using an immunocapture test has been relatively recently

commercialized. A Luciferase Immunoprecipitation System (LIPS) for the rapid detection of antibodies against PPR has also been recently developed.

Control

Antivirals have been suggested, but the generation of escape mutants is of concern. The standard disease control measures of quarantine, movement control, sanitary slaughter, and cleaning and disinfection are applied when the disease enters or re-appears in an area. The virus is susceptible to most disinfectants. Vaccines are used where the disease is established and it provides good immunity. Following the success of Rinderpest eradication, and in response to calls from member countries, FAO and OIE have taken the lead in developing a Global Strategy for the control and eradication of PPR. They believe PPR can be eradicated within 15 years, provided it is adequately resourced and well-coordinated, with the political commitment and participation of key partners.

Current vaccines for PPR

The current available PPR vaccines, are cell culture-attenuated strains of natural PPRV. The first vaccine, the Nigeria 75/1 has been used extensively in Africa and the Middle East, but other strains have also been developed, especially in India, where Sungri/96 is preferred. The OIE says that normally, the minimum immunising dose is 100x the lowest dose of vaccine virus able to induce 50% immunising response, and for Nigeria 75/1, the minimum titre is 102.5 TCID50. The vaccine is safe including in pregnant animals, and efficacious. It provides strong protective immunity for 3-5 years, enough to cover the lifespan of the small ruminants. It is effective against viruses from all lineages.

Research & Potential new vaccines and the way forward

The main challenges or the current vaccines are the thermostability and the DIVA capability. To improve the thermotolerance, two strategies have been used. One is by using different formulations and cycles during lyophilisation. The other one is the development of thermo-adapted strains. There are many publications or communications, each claiming that their method is the most appropriate. A comparison has been attempted in Table 8, but is not complete as information is not always clear or comparable. A priority would be the independent validation of the different techniques, starting from the same material and using the same equipment. This is something that PANVAC has been wanting to do for some time. The thermo-adapted strains developed at IVRI in India, are also very promising, and further validation might be warranted.

As for the DIVA vaccines, many strategies have been used. Various groups have been working on recombinant adenovirus expressing PPR. They are very promising candidates, but they need to be evaluated long term, as to confirm the life-long immunity with a single dose. Other strategies include the use of modified vaccinia virus

Ankara (requires 2 doses), virus like particles produced in baculovirus systems (have challenges for purification), recombinant fowlpox expressing PPR (poor response), DNA vaccines or plant expressed PPR proteins, both of which need further validation.

Combined vaccines are an asset, as one of the main costs of vaccination is logistics. It has been demonstrated that PPR and Sheep and Goat pox can be combined, and a commercial product already exists as a combination in Morocco. Recently this combination vaccine has started to be used in other African countries.Combined DIVA vaccines have double attraction. A very promising candidate is a Capripoxvirus expressing the PPR proteins, but has recently been shown to induce only partial protection for PPR in the presence of pre-exisiting immunity to the vector. With the use of reverse genetics, a recombinant PPR virus expressing Foot and Mouth Disease (FMD) protein has demonstrated protection from challenge with FMD virus, but is yet to be evaluated for challenge to PPR.

Commercial manufacturing of PPR vaccines

There are many commercial manufacturers of PPR vaccines in Asia and Africa. Their main interest at the moment, is improving thermotolerance of the current vaccine.

Clinical disease overview

Etiology & Epidemiology

The infective agent was first considered a variant of rinderpest virus adapted to small ruminants, but was later shown to be antigenically and genetically distinct. PPR is caused by a Morbillivirus in the family Paramyxoviridae. It is related to rinderpest, measles and canine distemper. PPRV is a pleomorphic particle (Figure 1) with a lipid envelope enclosing a ribonucleoprotein core that contains the genome, a single strand of RNA with negative polarity. The genome length of PPR virus (PPRV) is 15,948 nucleotides. There are six genes, or transcription units (Figure 1). The viral genes encode the nucleocapsid (N) protein, the phosphoprotein (P), the matrix protein (M), the fusion (F) and haemagglutinin (H) membrane glycoproteins, and the large protein (L), which is the viral polymerase. The P gene also encodes the three accessory proteins V, W and C, which are sometimes referred to as non-structural, although it is not conclusively proven that they are not part of the virion. They are not required for the replication and assembly of the virus. The P and L proteins together form the functional viral RNA polymerase. The F and H proteins are found in the viral envelope, projecting to the outside of the virion and the infected cell. The H protein is responsible for binding to the host cell receptor,

Virus structure

The PPRV glycoproteins (F and H) are embedded within the viral envelope. The M protein lines the inner surface of the virus envelope. The ribonucleoprotein complex is composed of N, P and L proteins in association with the RNA genome. Source: Parida et al, 2015 [2]

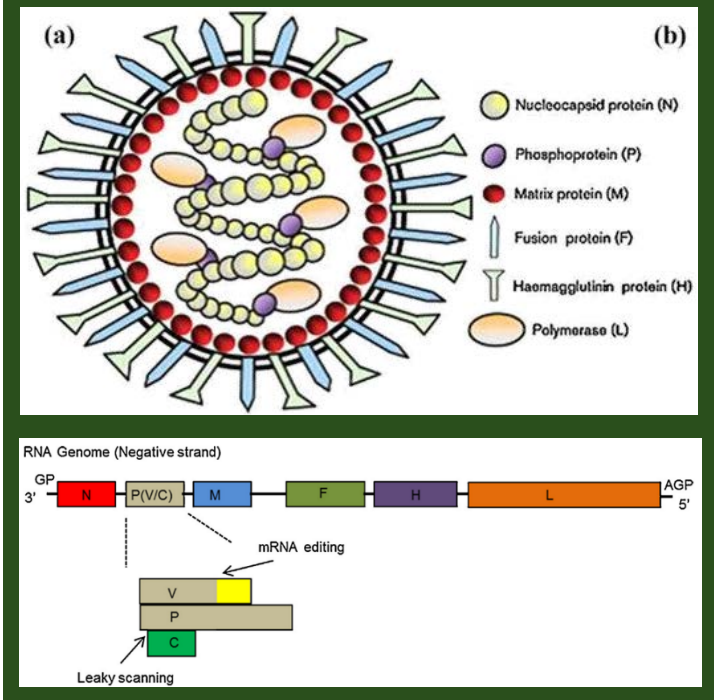

Figure 1: Schematic diagram of Peste des petits ruminants virion structure.

whereas the F protein allows the viral envelope to fuse with the host cell envelope, transferring the nucleocapsid to the host cell cytoplasm. The M protein plays an as-yet not understood role in virus budding and structure [1].

All PPR virus strains belong to a single serotype, but the different strains have been grouped into four distinct lineages, with lineages I and II occurring in West Africa, lineage III in East Africa, the Middle East and southern India, and lineage IV in Asia. These lineages are based on sequence differences on a short (approximately 300 bases) specific section of the viral F gene or N gene. The utility of lineage identification lies in the information it provides on the probable origin of the virus causing a new outbreak. PPRV lineage IV has been found in recent years in sub-Saharan Africa, and appears to be displacing viruses of the so-called “African” lineages (I–III). The disease occurs in a band that spreads across Africa between the equator and the Sahara, through the Arabian Peninsula, the Middle East, south-west Asia and India. China first reported the disease in 2007 and it spread into North Africa for the first time in Morocco in 2008 (see Figure 2).

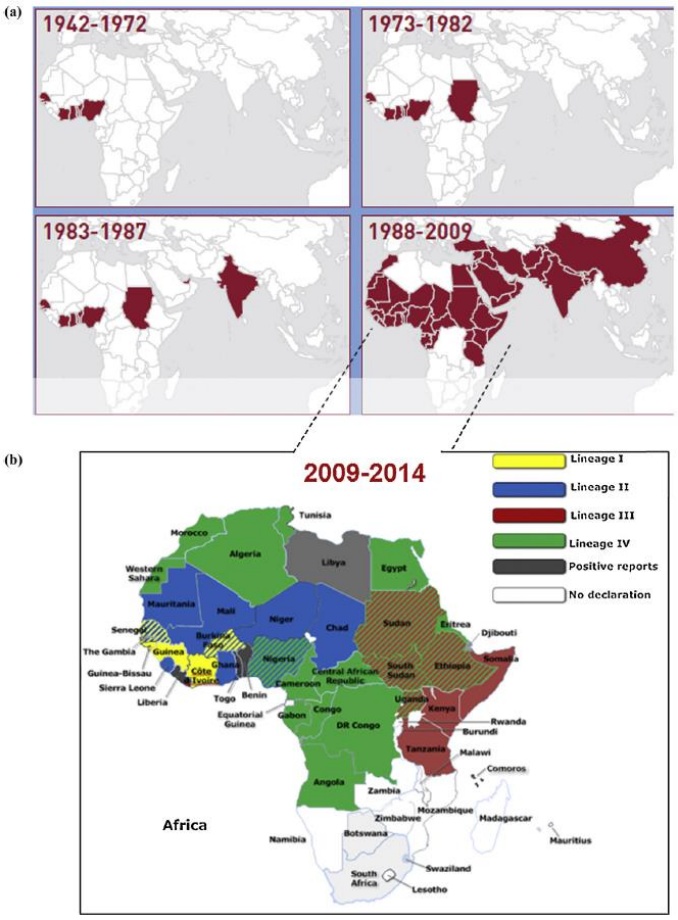

Figure 2: Global spread of PPR from its first detection in 1942-2014, including lineage distribution. Source: Parida et al, 2015 [2].

Hosts

Goats and sheep are the primary hosts for PPRV with few reports of disease outbreak in camels. Cattle, buffalo and pigs develop subclinical infection but are not capable of excreting the virus, and thus are not considered to be important in the epidemiology of the virus [2]. Infection of various wildlife species (mainly wild ungulates), has been reported, but there is limited information on species susceptibility and the occurrence of the disease.

Clinical Signs

Disease severity depends on various factors: PPRV lineage, species, breed, immune status of animals. Various clinical manifestations of the disease have been described in the literature. Young animals are most severely affected, and goats are more severely affected than sheep. In its most severe form (peracute) animals are found dead. However, the disease can be mild or unapparent and circulate in a country causing little or no illness until susceptible goats are exposed. Outbreaks tend to be associated with contact of immuno-naïve animals with animals from endemic areas. In addition to occurring in extensive-migratory populations, PPR can occur in village and urban settings though the number of animals is usually too small to maintain the virus in these situations.

- Morbidity rate in susceptible populations can reach 90–100%
- Mortality rates vary among susceptible animals but can reach 50–100% in more severe instances
- Both morbidity and mortality rates are lower in endemic areas and in adult animals when compared to young animals.

Three forms of clinical PPR are identified, namely:

Acute form

After an incubation period of 3-6 days, there is a sudden onset of fever, severe depression, loss of appetite, and clear nasal discharge. The serous nasal discharge becomes mucopurulent and resulting, at times, in a profuse catarrhal exudate which crusts over and occludes the nostrils causing respiratory distress. There is congestion of the conjunctiva, crusting on the medial canthus and sometimes profuse catarrhal conjunctivitis, causing eyelids to mat together with discharge. Tissues in the mouth can swell and ulcers form on the lower gums, dental pad, hard palate, cheeks and tongue. Necrotic stomatitis with halitosis is common. Erosions may resolve or coalesce. Severe watery, blood-stained diarrhoea develops in some animals, resulting in dehydration and weight loss. Pneumonia evidenced by coughing is common in later stages. Pregnant animals may abort. The prognosis is poor and death can occur within five to ten days of the onset of fever.

Peracute form

- Frequent in goats, especially in situations of PPRV introductions into immuno-naïve flocks.
- High fever, depression and death.
- Higher mortality.

Subacute form

- Frequent in some areas because of local breed susceptibility, form commonly seen in experimentally infected animals.
- Usually 10–15 days' development with inconsistent signs; on or about 6th day post-infection, fever and serous nasal discharge is observed.
- Fever falls with onset of diarrhoea and, if this is severe, may result in dehydration and prostration.

Seasonal variations

More frequent outbreaks are observed during the rainy season or the dry cold season. Also associated with seasonal periods of increased local trade in goats.

Transmission

Infected animals can transmit the virus to close in-contact susceptible animals through exhaled aerosol or clinical excretions (lacrimal, nasal, saliva, feces). Water, feed troughs, and bedding can also be contaminated with secretions and become additional sources of infection, however the virus does not survive for a long time outside the body of a host animal. The virus is temperature sensitive and readily inactivated in a dry environment. Infected animals that recover from disease develop a lifelong protective immunity and no carrier state has been identified. However, virus can circulate in animals with mild disease, leading to disease outbreaks, during which naïve susceptible populations are mixed with those infected and displaying a mild form of disease

Diagnosis

Table 1 summarizes the currently OIE recommended test methods available for the diagnosis of PPR and their purpose.

Identification of the agent

Agar gel immunodiffusion

- Simple and inexpensive test that can be performed in any laboratory and even in the field
- Standard PPR viral antigen is prepared from mesenteric or bronchial lymph nodes, spleen or lung
- Results are obtained in one day, but the test is not sensitive enough to detect mild forms of PPR due to the low quantity of viral antigen that is excreted.

Counter immunoelectrophoresis

- Most rapid test for viral antigen detection

Imunocapture enzyme-linked immunosorbent assay (icELISA)

- There is one commercial kit, which is available from OIE PPR Reference laboratories. It is reliable where local technology cannot perform molecular techniques, although it is not as sensitive as PCR.
- Using two monoclonal antibodies (MAb) raised to the N protein, allows a rapid identification of PPRV
- Sandwich ELISA is widely used in India

Nucleic acid recognition methods

- Reverse transcription PCR (RT-PCR) techniques based on the amplification of parts of the N and F protein genes have been developed for the specific diagnosis of PPR.
- Multiplex RT-PCR based on the amplification of fragments of N and M protein genes, has been reported.
- A real time RT-PCR, or Quantitative RT-PCR (QRT-PCR) assay has been developed for the specific detection of PPRV. It can detect all four lineages of the virus; QRT-PCR is ten times more sensitive than the classical RT-PCR.
- LAMP techniques have also been described.

Culture and isolation methods

- Even when diagnosis has been carried out by rapid techniques, the virus should always be isolated from field samples in tissue cultures for further studies.
- PPRV may be isolated in primary lamb kidney/ lung cells and some cell lines (Vero, B95a)

Table 1: Tests recommended by the OIE (OIE Terrestrial Manual of Diagnostic tests and vaccines for terrestrial animals 2015) and their purpose.

Method	Purpose				
	Population freedom from infection	Individual animal freedom from infection	Confirmation of clinical cases	Prevalence of infection - surveillance	Immune status in individual animals or populations post-vaccination
Competitive ELISA	**++**	**++**	**-**	**+++**	**+++**
Virus neutralization	+++	+++	-	+++	+++
RT-PCR	-	-	+++	-	-
Real Time RT-PCR (QRT-PCR)	-	-	+++	-	-
Virus isolation in cell culture	-	-	+++	-	-
Immunocapture ELISA	-	-	+++	-	-
Agar gel immunodiffusion	-	-	+	-	+
Counter immunoelectrophoresis	-	-	+	–	–

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – = not appropriate for this purpose.
Although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.

Serology

Virus neutralisation (the prescribed test for international trade)

- Test is sensitive and specific but time-consuming

Competitive enzyme-linked immunosorbent assay

- Several competitive ELISAS (C-ELISA) have been described based on the use of MAbs that recognise virus proteins.

Recent developments

A field test for PPRV has recently been developed at Pirbright Institute. This commercially available test is essentially a lateral flow device-formatted immunocapture test, and has been trialled in the field and found to be functional [3]. The test is based on the specificity and affinity of monoclonal antibody C77; this antibody recognizes the PPRV H protein, but not that of the related ruminant morbillivirus rinderpest.

A Luciferase Immunoprecipitation System (LIPS) for the rapid detection of antibodies against PPRV in serum samples and for specific differentiation from antibodies against Rinderpest (RP) virus has been recently developed. PPR and RP serum samples were assayed by PPR-LIPS and two commercially available PPR cELISA tests. The PPR-LIPS showed high sensitivity and specificity for the samples tested and showed no cross reactivity with RPV unlike the commercial PPR cELISA tests which did cross react with RPV. Based on the results, PPR-LIPS is presented as a good candidate for the specific serosurveillance of PPR [4].

Differential diagnosis

Peste des petits ruminants can be confused with other diseases such as rinderpest, bluetongue and contagious caprine pleuropneumonia, due to the similarity of these diseases in clinical signs. Contagious ecthyma, FMD, heartwater, coccidiosis and mineral poisoning might also be considered. Diagnosis of the disease may also be complicated, as the result of secondary bacterial infections specifically caused by Mannheimia haemolytica.

Immune response

PPRV is highly lymphotropic and infection often leads to a profound immunosuppression that causes leucopoenia and reduced antibody responses. Immunosuppression by PPRV has been observed in both vaccinated and infected animals. Virulent strains of the virus cause marked immunosuppression, whereas vaccination only induces a transient leucopoenia with no significant effects on the immune response [2].

Cellular and humoral immune responses are induced by infection but are also features of vaccination with the live attenuated vaccines that are available. The relative importance of humoral (antibody) and cell-mediated (cytotoxic T cell) responses in the recovery from infection with PPRV is not clear. Animals that recover from infection (including infection with the attenuated vaccine strains of PPRV) have high levels of circulating neutralising antibody as well as antigen-specific proliferating CD4+ T cells. The protective immune response of the host to PPRV infection is, in any event, obscured to some extent by the generalized immunosuppression common to infections with any of the morbilliviruses [1].

Maternal antibodies against the virus can be detected in young animals and remain able to neutralise virus for three to four months enabling a level of protection in newborn animals.

Sheep and goats vaccinated with an attenuated strain of PPR or that recover from PPR develop an active immunity. It is assumed that this protection is actually lifelong, as Rinderpest vaccine was observed to protect cattle (a naturally longer living species) for up to 10 years. For this reason, animals that have recovered from PPRV infection are assumed to be protected from the disease for life, although there are no published studies on attempts to re-infect animals that have recovered from the disease [1].

Incidence and Prevalence in Selected Countries

Global

Since its first identification in the early 1940s in Côte d'Ivoire, PPR has steadily expanded its geographical distribution beyond its original endemic region in Western Africa. It occurs now in most African countries from North Africa to Tanzania. A significant and dramatic geographical expansion of the disease has occurred over the last 15 years resulting in large parts of Central Asia, South Asia and East Asia now being endemic for PPR (Figures 2 & 3). It is present in the Arabian Peninsula, and nearly all Middle Eastern countries up to Turkey. Recent incursions into China (Tibet) and Morocco have caused serious disease outbreaks and disease has been reported to be moving southwards in East Africa.

Currently around 70 countries have reported infection to the OIE or are suspected to be infected and another 50 are considered at risk for PPR. Out of these infected countries, more than 60% are in Africa (including North Africa) the other infected countries being in Asia (South East Asia, China, South Asia and Central Asia/West Eurasia including Turkey) and the Middle East.

There is an OIE established procedure to recognise countries free of PPR. The latest official status as of May 2015 can be seen in the following link: http://www.oie.int/en/animal-health-in-the-world/official-disease-status/peste-des-petits-ruminants/list-of-ppr-free-members/. Officially PPR free countries in Asia and Africa include: Mauritius, Myanmar, Philippines, Singapore, South Africa, Swaziland and Thailand.

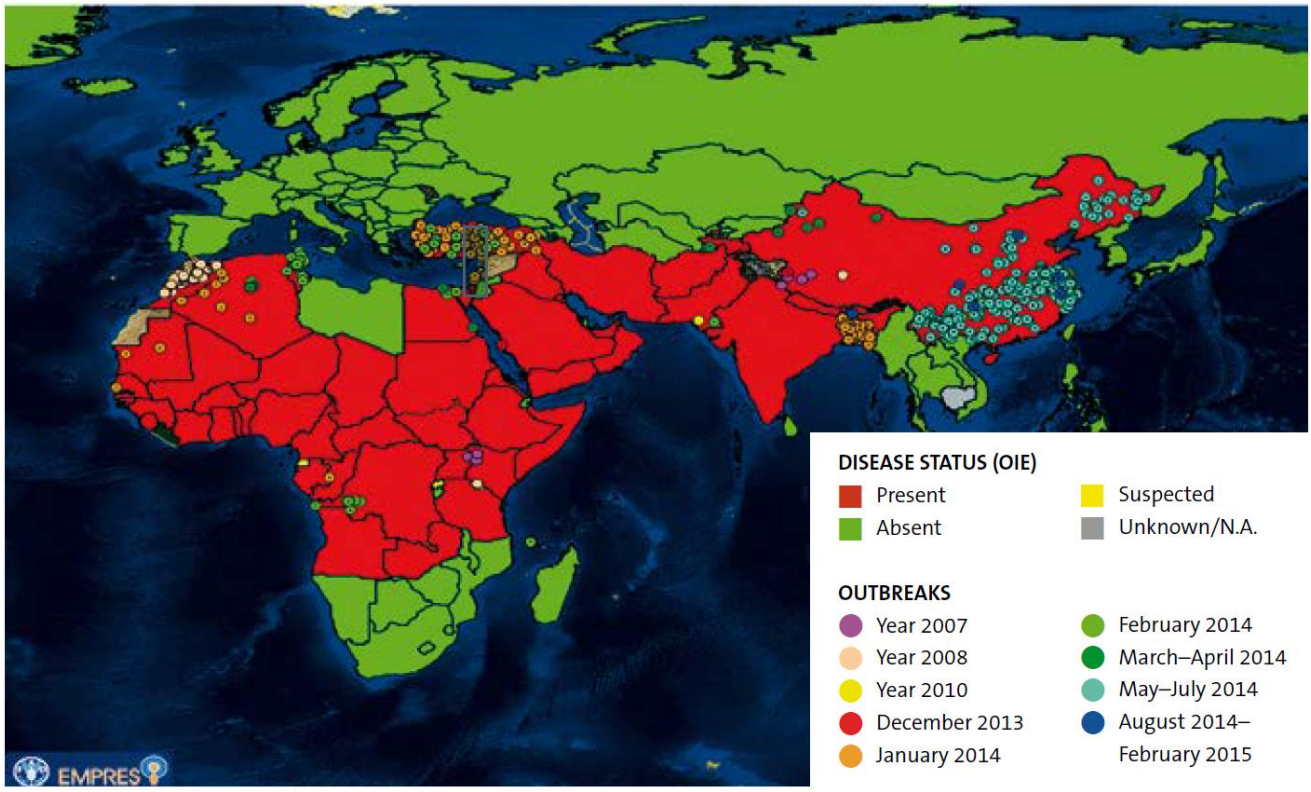

Figure 3: Global PPR situation and occurrence of outbreaks between 2007-2014. (Source: Global strategy for the control and eradication of PPR. FAO/OIE 2015.)

Regional

There are two main sources, OIE and AU-IBAR (which includes only Africa), but data are not always similar.

1st Source: OIE.

Data of outbreaks reported to the World Animal Health Organization (OIE) are shown in Tables 2 and 3. Data are not always reliable, as many countries do not seem to report, or to be reporting consistently over time.
http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/statusdetail

Similar information but presented in a different manner can be seen in Annex 1.

Number of cases reported to the OIE by disease and by country:

- No information, + Present but quantitative data not known, ? Disease suspected

Table 2: ASIA – PPR outbreaks notified to OIE from the Asian countries of interest.

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Bangladesh	-	-	+	+	+	+	+	+	+	+	-
India	1,071	507	434	165	184	300	197	128	123	82	-
Indonesia	0	0	-	0	0	0	0	0	0	-	-
Myanmar	0	0	0	0	0	0	0	0	0	0	-
Nepal	51	174	320	>13	143	179	121	98	25	41	27
Vietnam	0	0	0	0	0	0	0	0	0	0	0

Note: Myanmar has OIE official freedom status.

Table 3: AFRICA – PPR outbreaks notified to OIE from the Asian countries of interest.

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	+	+	+	>12	2	5	7	11	1	17	2
Ethiopia	41	115	54	67	75	113	85	103	116	44	-
Ivory Coast	3	0	+	>2	17	19	28	7	8	24	10
Kenya	0	10	3	0	+?	+?	+?	+?	4	29	8
Madagascar	0	0	0	0	0	0	0	0	0	0	-
Malawi	0	0	0	0	0	0	0	0	0	-	-
Mali	1	4	3	1	?	-	3	0	2	1	-
Mozambique	0	0	0	0	0	0	0	0	0	0	-
Rwanda	-	0	0	?	0	?	?	?	?	-	-
Senegal	9	5	7	28	25	6	9	5	9	4	1

South Africa	0	0	0	0	0	0	0	0	0	0	-
Tanzania	0	0	0	1	> 2	>2	>2	>1	2	2	4
Uganda	0	0	1	9	2	+	+	1	+	+	-
Zambia	-	0	-	-	0	+?	0	0	0	0	-

Note: South Africa has OIE official freedom status.

2nd Source: AU-IBAR.

Number of outbreaks per year as reported to AU-IBAR and published in the Pan African Animal Resources Yearbook. (**http://www.au-ibar.org/pan-african-animal-resources-yearbook?showall=&limitstart**=). Table 4 shows the number of PPR outbreaks reported to AU-IBAR. Below the table, there are some relevant notes for specific years that were included in the AU-IBAR reports.

Table 4: Number of PPR outbreaks per year as reported to AU-IBAR and published in the Pan African Animal Resources YearBook. Please see notes below the table for each year (NS= Not specified)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso				12	2	5	7	10	1	17	
Ethiopia	20		111	252	1	144	111	154	270	83	
Ivory Coast	2	2			17	17	28	11	2	24	
Kenya		NS	4					4		9	
Madagascar											
Malawi											
Mali				3			3		2	1	
Mozambique											
Rwanda											
Senegal	4	6	13	31	32	2	5	6	9	4	

South Africa											
Tanzania						NS	2	1	2	2	
Uganda		NS	5	2			4	1	8	2	
Zambia											

First reports of PPR in Kenya were in March 2006, in North Turkana District. In Uganda, the PPR outbreak started in 2006. The disease has been showing geographical advances towards the southern and northern regions of Africa with Tanzania (2008) and Zambia (2010) in the south and Algeria (2011). Egypt became infected in 2012.

Prevalence data by country

- Sources: PubMed, and internet engine searches (English and French when applicable).
- Efforts have been made to include the year of the study, and not the year of the publication. If they are known to be different, the year of publication is included in the reference.
- Note that not all papers have been read in full. In many cases, only the abstracts have been read. Critical evaluation of the papers for inclusion has not been conducted. If a review paper included some references, the source of the review is mentioned.

ASIA

Bangladesh

Year	Area	Species of animal	No. samples tested	% positive	Reference
2014	Upazila Veterinary Hospital, Thakurganon	Goats	132	39	Bupasha et al, 2015
2012-2013	Chittagong District	Goats	5,485	8.99	Parvez et al, 2014
2012	Upazila Veterinay Hospital, Cox's Bazar.	Goats	182	47	Islam et al, 2014
2010-2011	Rajshahi District	Goats	627	20.57	Sarker and Islam, 2011

2010	Upzilla Veterinary Hospital, Mohammadpur, Magura	Goats	209	5.3	Karim et al, 2014
2010	Sujanagar, Sathia and Bera, Pabna district	Goats	6,408	2.18	Rahman et al, 2011
2010	Mirzaganj upazila, Patuakhali District	Goats	183	50.27	Islam et al, 2012
2008	Upazila Veterinary Hospital, Kushtia Sadar	Goats	280	12.5	Sharifuzzaman et al, 2015

India

Year	Area	Species of animal	No. samples tested	% positive	Reference
2013-2014	North-East India	Goats	391	17.90	Balamurugan et al, 2014
2012	Gujarat	Sheep, goats, cattle, buffaloes and camels	Sheep: 355, Goats: 141, Cattle: 80, Buffaloes: 115, Camels: 65	Sheep: 41.12, Goats: 26.95, Cattle: 11.25 Buffaloes: 14.78 Camels: 12.30	Pradip et al, 2012
2011	52 districts in 5 states (AP, Gujuarat, Jammu and Kashmir, Maharashtra and Rajasthan)	Cattle, buffalo, sheep and goats	Cattle: 605 Buffaloes: 432 Sheep: 173 Goats: 288	Cattle: 11.07 Buffaloes: 16.20 Sheep: 45.66 Goats: 38.54	Balamurugan et al, 2014
2009-2010	Southern peninsular India	Cattle and buffaloes	Cattle: 1,158 Buffaloes: 1,001	4.58	Balamurugan et al, 2012
2003-2009	Samples submitted to IVRI	Sheep and goats (see table below for details)	Sheep: 2,197 Goats: 2,687	Sheep: 41.01 Goats: 46.11	Balamurugan et al, 2011

State	Sheep			Goats		
	Tested	Number positive	Percentage positive	Tested	Number positive	Percentage positive
Andhra Pradesh	10	10	100.00	0	0	0.00
Assam	0	0	0.00	119	0	0.00
Gujarat	228	43	18.85	395	167	42.27
Haryana	0	0	0.00	45	22	48.89
Himachal Pradesh	87	8	9.19	230	57	24.78
Jammu & Kashmir	129	63	48.84	201	103	51.24
Karnataka	199	58	29.15	40	26	65.00
Maharashtra	616	365	59.25	575	336	58.43
Rajasthan	630	252	40.00	205	132	64.39
Tripura	0	0	0.00	13	13	100.00
Uttar Pradesh*	298	102	34.23	859	379	44.12
West Bengal	0	0	0.00	5	4	80.00
Total	**2,197**	**901**	**41.01 ± 8.86** (CI: 23.65 to 58.37)	**2,687**	**1,239**	**46.11 ± 8.53** (CI: 29.39 to 62.83)

Seroprevalence of peste des petits ruminants in sheep and goats by state for the 2003–2009 period. Source: Balamurugan et al, 2011

Indonesia

The disease has never been reported in Indonesia. Source: **Sendow, 2014**.

Nepal

No information on the prevalence of PPR in Nepal was found.

Vietnam

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2006-2008?	Ha Giang province	Goats	283	1	Maillard et al, 2008

AFRICA

- The disease has never been reported in Madagascar, Malawi, Mozambique and South Africa.
- No information has been found for Ivory Coast, Rwanda and Senegal.
-

Burkina Faso

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2005	9 Departments Soum Province	Goats and sheep	Goats: 878 Sheep: 1,236	Goats: 23.01 Sheep: 33.09 (Details in table below)	Sow et al, 2008

Département	Nb. de sérums	Nb. positifs	Prévalence (%)
Aribinda	250	9	3,60
Baraboulé	250	111	44,40
Diguel	200	5	2,50
Djibo	250	111	44,40
Kelbo	204	14	6,86
Koutougou	260	86	33,08
Nasoumbou	250	180	72,00
Pobé Mengao	200	25	12,50
Tongomayel	250	70	28,00
Total	2 114	611	28,90

Prevalence anti-PPR antibodies per department in Soum Province. Source: Sow et al, 2008

Ethiopia

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Dassenech (South Omo)	Sheep and goats	Sheep: 77 Goats: 184	Sheep: 49 Goats: 42	Molla and Delil, 2015
2012	Awash Fentale	Sheep and goats		Before outbreak: 7.3 After outbreak: 42.6	Delil et al, 2012
2006-2007	Awash Fentale District, Afar	Sheep and goats	1,239	1.70	Faris et al, 2012
2001	Afar, Borena, East Shewa, Gambela, Jijiga	Various	Camels: 628 Cattle: 910 Goats: 442 Sheep: 835	Camels: 3 Cattle: 9 Goats: 9 Sheep: 13	Abraham et al, 2005
1999.	43 weredas across the country	Goats and sheep	13,651	6.4	Waret-Szkuta et al, 2008

Kenya

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2011	Turkana	Sheep and goats	Sheep: 431 Goats: 538	Sheep: 32 Goats: 40	Kihu et al, 2015

Tanzania

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Ngorongoro District	Various wild animals	Buffalo: 10 Grant's gazelle: 30 Thomson's gazelle: 1 Wildebeest: 2 Impala: 3 Goats: 5 Sheep: 5	Buffaloes: 50 Grant's gazelle: 66 Th. Gazelle: 0 Wildebeest: 50 Impala: 100 Goat: 40 Sheep: 0	Mahapatra et al, 2015
2014	Ngorongoro, close to Mahenge and Mikumi.	Sheep and goats	Sheep: 236 Goats: 242	Sheep 43.2 Goats: 49	Herbe, 2015
2011	Mtwara region	Goats and sheep	216	31	Muse et al, 2012
2011	Ngorongoro District	Cattle and buffalo	Cattle: 266 Buffaloes: 150	Cattle: 17.3 Buffaloes: 0	Lembo et al, 2013
2009	Ngorongoro, Monduli, Longido, Karatu, Mbulu, Siha and SImanjiro	Sheep and goats	Sheep: 657 Goats: 892	Goats: 49.5 Sheep: 39.8	Swai et al, 2009
2009	Mtwara and LIndi	Sheep and goats	Goats: 434 Sheep: 70	Goats: 28.7 Sheep: 35.7	Mbyuzi et al, 2014
2008-2009	12 districts Arusha, Kilimanjaro, Manyara and Tanga	Sheep and goats	Goats: 2,182 Sheep: 1,296	Goats: 0.22 Sheep: 0.22	Kivaria et al, 2013

The disease was first reported in 2008.

Uganda

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Makindye, Rubaga, Nakawa, Kawempe, Wakiso, Greater and Central Kampala	Goats	190	1.6	**Lernfelt, 2013**
2009	Moroto, Nakapiripirit, Abim and Kotido	Goats	Morotoe: 87 Nakapiripirit: 52 Abim: 1 Kotido: 80 Total: 280	Moroto: 63.2 Nakapiripirit: 72 Abim: 1.6 Kotido: 85.2 Total: 57.6	**Mulindwa et al, 2011**

Zambia

There was an outbreak reported in May 2015. The previous outbreak was when the disease was first reported in 2010. Source: **Pro-med**. There are no reports available on prevalence.

Economic and Social Impacts at Global and Regional Levels, and in Selected Countries

FAO and OIE during 2015 unveiled the Global strategy for the control and eradication of PPR [5][6], in which the organizations noted that PPR is present in around 70 countries in Africa, the Middle East and Asia, threatening more than 1.7 billion of the total global population of 2.1 billion sheep and goats, as well as the livelihoods, food security and nutrition of more than 330 million people in these regions – mainly poor farming communities that rely solely on small ruminant production for their survival. Another 50 countries are at risk of incursions of the disease from neighbouring areas, threatening an additional 167 million sheep and goats.

Morbidity, mortality and production

In the worst situations, PPR-related morbidity is 100%, with up to 90% mortality. In areas where the disease is endemic, the mortality rate may be lower; yet the disease has an insidious impact, hampering the development of lambs and kids and compromising the immune defense of adult animals against other diseases. The rates depend on methodology used in data collection, species and farming systems, as exemplified by Kimani et al, 2015, Socio-economics of PPR presentation at FAO and OIE Conference for the control and eradication of PPR in Abidjan:

- In endemic countries morbidity rates range from 6.2 to 65% in Somalia and 48.4 to 56.6% in Cote d'Ivoire
- During epidemics these rates rise to between 86 to 100% (reported in Kenya, Ethiopia and Eritrea)
- Mortality rates also vary with reports - 0-97% in Cote d'Ivoire; 69 to 74% in Tanzania; 33 to 90% in Kenya, Ethiopia and Eritrea
- Two studies from India indicate that while the mortality rate was relatively low per animal affected, the overall losses were high even when the animal recovered

As for effects on production, Kimani et al, also mentioned:

- In Tanzania it was estimated that 330,910 kids/lambs were not born due to abortions.

- In Kenya and Tanzania 10% of households lost their entire herd or flock
- It was estimated that in Kenya, Tanzania and Somalia milk production losses were in the region of 2 million litres

Overall, PPR is a limiting factor to the development of healthy and thriving flocks and herds.

Economic impact

Rushton et al, present in Annex 1 of the PPR Global strategy already mentioned, the details of the socio-economic impact of PPR. They estimate the direct annual losses due to PPR between USD 1.2 and 1.7 billion. The estimated current expenditure on PPR vaccination ranges between USD 270 and 380 million. The annual impact of PPR alone may be valued at between USD 1.45 and 2.1 billion per year. This was estimated using the assumptions that two thirds of the animals affected would die, and that would mean a loss of USD 35 per animal that dies, and USD 3.50 per animal affected that recovers. The cost of vaccination was estimated at USD 0.80 per dose delivered (cost of the dose, and the time of the people involved). A sensitivity analysis included the value of a dead animal at USD 50, and USD 5 for an animal that recovered. Approximately a third of the global financial burden of PPR is borne by Africa, with a further quarter borne by South Asia (see Figure 4).

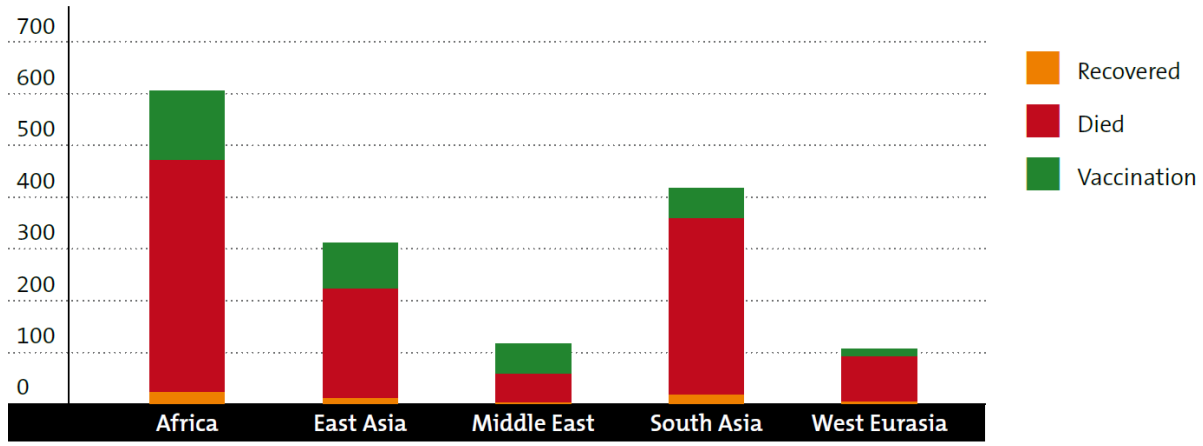

Figure 4: Impact of PPR in USD millions. Source: Global strategy for the control and eradication of PPR. FAO and OIE, 2015.

Economic rationale for global control

The estimated maximum undiscounted costs for a fifteen-year global PPR strategy is between US$7.6 and US$ 9.1 billion with the first five years costing between US$ 2.5 and 3.1 billion (Rushton et al, 2015. Annex 5 – Costing of the PPR global control and eradication strategy, in FAO & OIE Global strategy for the control and eradication of PPR). The lower range is 16.5% less and would be expected as a consequence of a rapid decrease in PPR incidence in countries employing an effective vaccination strategy. In all scenarios tested there are significant vaccination campaigns that could well be reduced with strong targeting of at risk populations through carefully epidemiological and economic analysis. These costs have also given a realistic figure on vaccine dose costs and an amount to cover the delivery costs in different scenarios. These costs need to be placed into the perspective of the numbers of animals that are being protected by the measures proposed – nearly a billion sheep and a billion goats. A rough estimate of the average cost per shoat per year would mean an investment of between US$ 0.27 and 0.32.

The current annual impact alone of PPR is between US$1.45 to 2.1 billion per year, and with a successful eradication program this impact would be reduced to zero. A control and eradication program at an estimated cost of USD 2.5 billion (undiscounted costs) over an initial 5-year period (i.e. approximately USD 0.5 billion per year) appears small in comparison. A reduction of 42% in the impact of PPR would justify the annual expenditure alone. It is important to recognize that without the strategy anything between US$ 4.0 and 5.5 billion would be spent over a fifteen-year period on poorly targeted vaccination campaigns that is unlikely to lead to eradication. In summary the global spending in the current structures will cost between US0.14 to 0.20 per sheep or goat year which will not result in eradication.

Country examples (focus on countries of interest)

1. India

- **Thombare and Sinha in 2009**, reported on a cross-sectional sample survey conducted across six villages severely affected by PPR disease in the Pune district of Maharastra, during 2005-6. The incidence and mortality rate were found slightly higher in sheep than goats. The total losses due to disease ranged from Rs 918 in sheep (USD 19 using exchange rate of June 2009) to Rs 945 in goats (USD 19.4). Reduction in the market value of animals was recorded as the major loss component as appearance of the animal changes drastically after the illness, costing Rs. 404 (USD 8.3 - 44 %) in sheep and Rs 408 (43%) in goat, and this was followed by losses in production yield. Expenditure on medicine and infertility was found to cause more than 80 per cent of the total cost, followed by veterinary and labour services. The authors suggested that timely vaccination could be the best and low-cost preventive measure to control such deadly disease outbreaks.

- **Awase et al, 2013**, using primary data from villages of Indore division of Madhya Pradesh, calculated that the overall incidence rate in goat of Indore division was 8.7 % and mortality rate 3.2 %. The total economic losses due to PPR was found to be Rs.523 (approx. USD 8.76) per affected animal. The production loss due to reduced body weight comprised the maximum proportion and it was about Rs.278 (USD 4.6) accounted for 53.2 per cent of total loss. The economic loss in market price of goat due to poor physical appearance was Rs. 137 (USD 2.3) was the next most important, comprising nearly 26 per cent. The treatment cost which include medicine cost, registration or consultancy fee, miscellaneous expenses was Rs.108 (USD 1.8) per goat.

- **Singh et al 2015**, used 2 methodologies for their calculations. Based on data reported by the Government of India between 2008-2012, the study showed average annual economic loss of Rs. 167.83 lacs (approx. USD 345,000), of which Rs. 125.67 lacs (USD 258,000) and Rs. 42.16 lacs (USD 86,000) respectively are due to the incidence of the disease in goats and sheep. Morbidity losses constituted the greater share of the total loss in both goats and sheep (56.99% and 61.34%, respectively). Among different components of morbidity loss, direct body weight loss was the most significant in both goats and sheep. Based on cases and deaths as reported in sample survey studies, the estimated annual economic loss due to PPR in goats and sheep is Rs. 8895.12 crores (approx. USD 1,298 million), of which Rs. 5477.48 (approx. USD 799 million) and Rs. 3417.64 crores (approx. USD 498 millions) respectively are due to the disease in goats and sheep. The authors said that the calculations using the data from the Government of India were too low, probably on account of under reporting of cases and deaths.

2. Kenya

- **Kihu et al. 2015,** observed that PPR was a major economic disease affecting the pastoral herders in Kenya, with outbreaks in Turkana County having devastating effects on the Turkana livelihoods. The study estimated the direct economic losses occasioned by outbreaks of PPR based on perceived loss of benefits experienced by the Turkana people. They estimated the losses due to PPR at US$ 19.1 million and that mortality due to PPR constituted the greatest economic loss valued at US$ 16.8 million being 88% of the total losses. Other losses due to lost milk and weight loss constituted approximately 12% of the total losses. They concluded that PPR has serious economic impacts on pastoral livelihoods, and that previous estimation of PPR losses in Kenya was grossly undervalued.

Disease Prevention and Control Methods

Treatment (Control)

Currently, there are no medications available to treat the disease, but supportive treatment may decrease mortality. Antibiotics may help with secondary pulmonary infections.

Effective and rapid control of PPR is foreseeable using cheap antiviral compounds – they could be used to limit the clinical impact of PPR quickly in emergency situations while immunity by vaccination develops, in the context of introduction into a new area or re-emergence in endemic areas. Antivirals based on synthetic short interfering RNAs (siRNAs), a new class of molecules with a significant potential for therapeutic applications could be good candidates since they can be delivered in viral vectors and biologically synthesised in the treated animals. Servan de Almeida et al [7], described that nucleocapsid genes of PPRV and RPV can be targeted efficiently by siRNAs, resulting in a >80 % reduction in virus replication. However, along with the development of efficient RNAi-based therapeutics comes the risk of emergence of resistant viruses. Holz et al 2012 [8], challenged the in vitro propensity of PPRV, a stable RNA virus, to escape the inhibition conferred by single or multiple siRNAs against conserved regions of the N gene. Except with the combination of three different siRNAs, the virus systematically escaped RNAi after 3 to 20 consecutive passages. The genetic modifications involved consisted of single or multiple point nucleotide mutations and a deletion of a stretch of six nucleotides, illustrating that this virus has an unusual genomic malleability and that the generation of escape mutants with mutations in this region was unexpectedly easy.

Prophylaxis (Prevention)

When the disease appears in a previously unaffected area, the standard disease control measures consisting of quarantine, movement control, sanitary slaughter, and cleaning and disinfection are applied. The virus is susceptible to most disinfectants. Vaccines are used where the disease is established and it provides good immunity. For more details on the vaccine, see Section 6.

Sanitary prophylaxis

Epidemic outbreak situations: when the disease appears in previously PPR-free zones or countries.

- Rapid identification, humane slaughter and disposal of affected animals and their contacts; carcasses burned or buried
- Strict quarantine and control of animal movements
- Effective cleaning and disinfection of contaminated areas of all premises with lipid solvent solutions of high or low pH and disinfectants; includes physical perimeters, equipment and clothing
- Careful consideration to use of vaccine; strategic ring vaccination and/or vaccination of high-risk populations
- Monitoring of wild and captive animals

Endemic outbreak situations: when is continually circulating.

- Most commonly employed control mechanism is vaccination
- Sheep and goats vaccinated with an attenuated strain of PPR or that recover from PPR develop an active life-long immunity against the disease
- Monitoring of wild and captive animals; especially avoiding contact with sheep and goats
- Exposed or infected animals should be slaughtered and the carcases should be burned with deep burial.

Options and strategies for control programs at national, sub-national, regional and global level

A number of countries and regions have embarked on the control of PPR, often with assistance and/or advice from FAO and OIE. However, many of these national programs are inadequately resourced and poorly coordinated and could benefit significantly from a concerted, well-funded effort to make any impact.

Since 2011, FAO and OIE have supported the formulation of PPR control and eradication strategies for regions covered by the South Asian Association for Regional Cooperation (SAARC), Southern African Development Community (SADC), Intergovernmental Authority on Development (IGAD) and the African Union's Inter-African Bureau for Animal Resources (AU-IBAR).

An example of the control measures taken by some African countries to control PPR in 2008, can be seen in Figure 5. Number slaughtered means the number of animals killed for salvaging products partly or entirely for consumption or other use as part of a disease control strategy. Number destroyed refers to the number of animals killed and buried or burned as a means of disease control.

Country	Slaugh-ter	Destro-yed	Control Vac.	Prophy. Vac.
Benin	536	11	21522	0
C.A.R.	168	0	0	0
Congo	1	3	0	0
D.R. Congo	17	0	0	0
Eritrea	0	5	0	0
Ethiopia	36	0	424543	53742
Ghana	95	0	1538	0
Guinea	96	26	2307	0
Mali	50	0	4660	0
Nigeria	367	29	141763	78143
Sudan	0	0	952	59789
Togo	616	404	0	0
12 countries	**1982**	**478**	**597285**	**191674**

Figure 5: Control measures undertaken by affected countries during 2008 and some related quantitative data. Source: AU-IBAR Pan African Animal Health Yearbook, 2008.

Progressive control and eradication of PPR

In response to calls from member countries, FAO and OIE have taken the lead in developing a Global Strategy for the control and eradication of PPR [5][6] – See Figure 6. They believe PPR can be eradicated within 15 years, provided it is adequately resourced and well-coordinated at all levels, with the political commitment and participation of key partners. This is less than half the time it took to eradicate rinderpest. In addition, other high impact infectious diseases of small ruminants could be controlled, at a relatively small incremental cost, if linked to PPR control and eradication. These may include sheep and goat pox, brucellosis and contagious caprine pleuropneumonia.

The Global Strategy for the control and eradication of PPR has 3 integrated components:

1- PPR control and eradication
2- Strengthening veterinary services
3- Prevention and control of other major diseases of small ruminants

An overview of the objectives, outputs and other aspects of the strategy can be seen in Table 5.

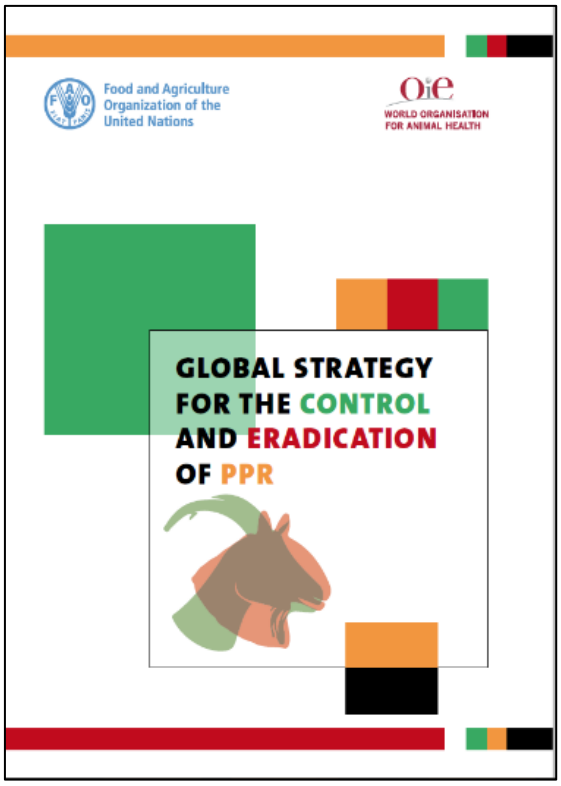

Figure 6: OIE and FAO Global strategy for the control and eradication of PPR (click on figure to follow the link)

Table 5: Overview of the FAO/OIE Global Strategy for the control and eradication of PPR. Source: FAO/OIE Global control and eradication of PPR – investing in veterinary systems, food security and poverty alleviation, 2015 [6]

Objectives	> Progressively reduce the incidence and spread of PPR and ultimately eradicate PPR > Ensure that previously non-infected countries remain free from the disease
Key outputs	> PPR eradicated globally > Improved control of other important diseases of small ruminants (e.g. goat and sheep pox, brucellosis and foot and mouth disease) > Enhanced capacity of Veterinary Services to control PPR and other livestock diseases > Improved efficiency in productivity of small ruminants in Africa, the Middle East and Asia
Societal impacts and outcomes	> Improved contribution of the small ruminant sector to food security and nutrition, food safety, public health and national economic development > Significant reduction in poverty through enhanced livelihoods of over 330 million poor livestock farmers in Africa, the Middle East and Asia
Main tools deployed	> Large-scale, vaccination in endemic countries with existing, live, attenuated, efficacious vaccines and establishment of regional vaccine banks > Surveillance and post-vaccination evaluation and monitoring using available diagnostic tests ensuring that vaccination results in increased flock immunity, reduced disease incidence and eventually reduced virus circulation and elimination > Evaluation of Veterinary Services capabilities and investment needs through the use of the Performance of Veterinary Services (PVS) Pathway tools, on a voluntary basis

The strategy is presented at 3 different levels: national, regional and global.

At **national level**, the strategic approach is based on 4 stages, corresponding to a combination of decreasing levels of epidemiological risk and increasing levels of prevention and control capabilities, as seen in Figure 7. In Stage 1 the epidemiological situation is being assessed, and in Stage 4, the country can provide evidence that there is no virus circulating either at zonal or national level.

At **regional level**, the focus is on regional coordination and harmonisation of national strategies and activities. Regional Economic Communities and other relevant regional organisations such as the African Union- Inter African Bureau for Animal Resources (AU-IBAR) in Africa are expected to play an important role.

At **global level**, will create a new Global Secretariat for the implementation of the Global PPR control and Eradication Program (PPR-GCEP).

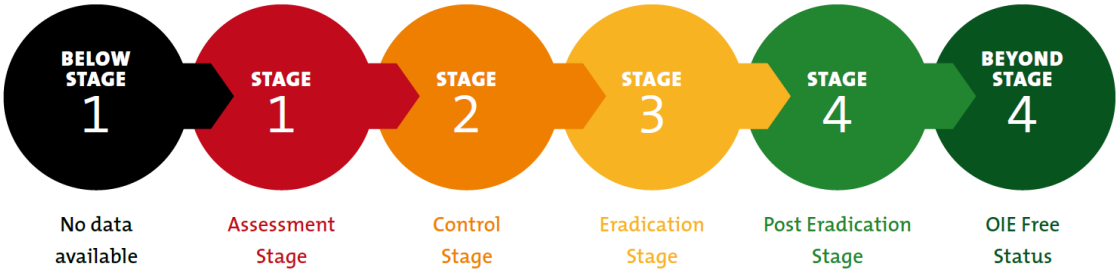

Figure 7: The progressive step-wise approach for the prevention and control of PPR. Source: Global strategy for the control and eradication of PPR, 2015. FAO & OIE [5].

Regional Roadmaps

The Global strategy has developed 9 regional roadmaps, which provide countries with a common long-term vision and create incentives for them to develop and embark on national risk reduction strategies with similar progress objectives, milestones and timelines (see Figure 8).

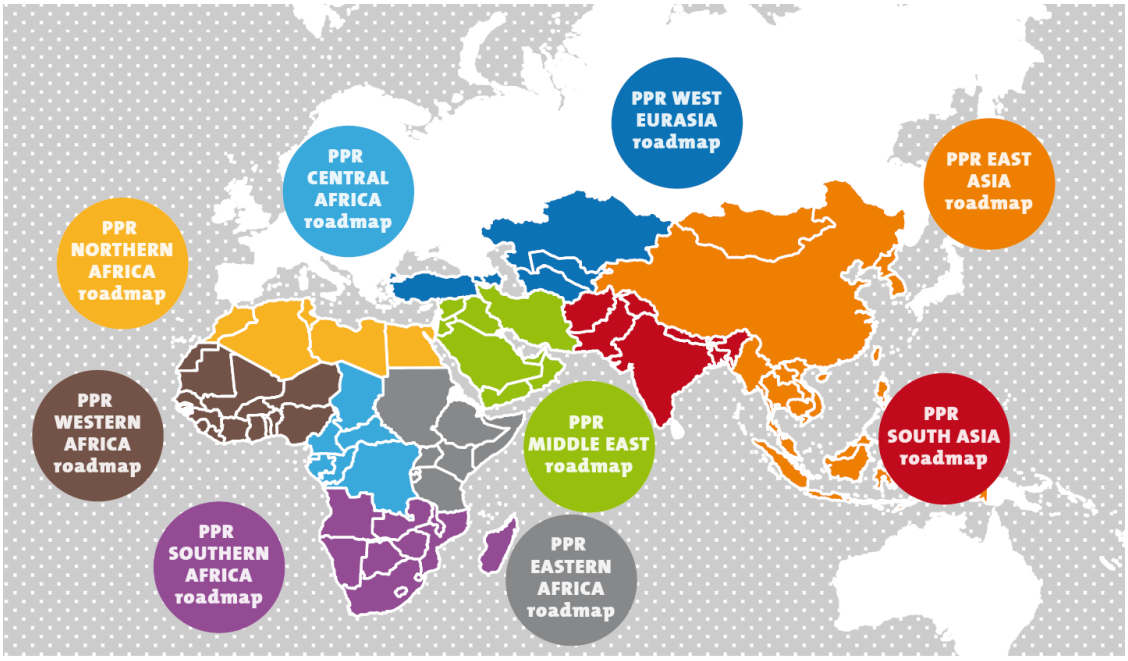

Figure 8: Regional Roadmaps for PPR control and eradication. Source: Global strategy for the control and eradication of PPR, 2015. FAO & OIE [5].

Regional situations for the areas that include the focus countries:

(as described in the 2015 Global Strategy for the control and eradication of PPR)

South Asia

In South Asia, a regional roadmap was formulated in 2011 by the SAARC member countries and it will be reviewed every two years. With the exception of Sri Lanka, all SAARC countries have reported PPR infection; however, the disease was reported only once in Maldives and Bhutan. Each SAARC country has a national laboratory suitable for PPR diagnosis and the Bangladesh national laboratory currently serves as the regional laboratory. Surveillance is ongoing as well as vaccination campaigns in high-risk-identified areas. Bangladesh, India and Nepal are producing PPR vaccine; however, there is an urgent need to improve the quality and quantity of these vaccines to meet national and regional requirements. At a regional meeting held in December 2013 several challenges were identified, including the lack socioeconomic impact assessment across the value chain, the need to develop a strategic plan and ensure a budget for its implementation and to enhance technical expertise and skills. Agreement was also reached on the need to raise awareness among farmers, to formulate or revise and enforce regulations regarding animal movements, to harmonize laboratory diagnostic tests in the region and to deliver quality assured vaccines. Some countries benefit from strong FAO technical support, such

as Afghanistan and Pakistan where disease surveillance, laboratory diagnostic capacities, vaccine production and vaccination campaigns are being strengthened.

Eastern Africa

In Eastern Africa all countries are infected and a regional strategy has been developed aimed at developing or improving a series of activities, including surveillance, diagnostic procedures, vaccination and awareness campaigns. Currently, prevention and control measures for PPR as well as other diseases are based on vaccination campaigns conducted mostly in response to disease outbreaks and hence are focused around the outbreak area (i.e. ring vaccination). Nevertheless, mass PPR vaccination campaigns were conducted in Kenya in 2008/2009 and Somalia in 2012/2013, and there are plans for conducting them in Ethiopia. The Nigeria 75/1 strain (produced in Ethiopia, Kenya and Sudan) was used in these vaccination campaigns. The use of a thermotolerant vaccine would be an important improvement for vaccination efficacy.

Southern Africa

Most countries in Southern Africa are currently free from PPR but the SADC member countries, after the introduction of PPR in a few countries, developed in 2010 a regional PPR control strategy.

Link: http://www.sadc.int/files/7413/5542/4349/PPR_Strategey.pdf

The main objectives of this strategy are as follows:

1. to immediately contain/control PPRV circulating in Angola, Democratic Republic of the Congo and Tanzania,
2. to prevent the disease from spreading to Malawi, Mozambique and Zambia,
3. to propose a methodology for the long-term eradication of PPR from the SADC region.

Currently, only Botswana produces PPR vaccines in the SADC region. South Africa has an OIE recognized official PPR free status. Support is being given by the FAO and IAEA to enhance laboratory diagnosis and vaccine production capabilities, improve disease surveillance, undertake socio-economic studies on PPR impact, and strengthen coordination/harmonization of PPR prevention and control in the region.

Central Africa and West Africa

All countries in Central and West Africa are infected. Regional meetings and conferences have already addressed the PPR issue (e.g. Conferences of the OIE Regional Commission for Africa) and FAO has implemented several national projects supporting activities in laboratory diagnostic (together with IAEA), surveillance and other field operations or vaccine production (together with AU-PANVAC), formulation of national strategic plans, etc.

Vaccination campaigns are undertaken in endemic and at-risk areas but the achievements are not always optimal.

A pilot field project funded by the Bill & Melinda Gates Foundation was carried out by the OIE in Ghana and Burkina Faso to identify the major constraints that may hamper the successful implementation of vaccination programs. Various productions systems and vaccine delivery systems (public and private) were considered in the study and several evaluation methods were tested. Logistical issues and communication directed at owners and vaccinators were among the principle factors that could determine positive achievements or failures. This field component was combined with two other components, namely the improvement of the quality of PPR vaccines produced in Africa, implemented by AU-PANCVAC, and the establishment of a vaccine bank. Currently, Niger, Nigeria, Mali and Senegal are PPR vaccine producers. At the regional level, a number of limiting factors have been recognized, such as the efficacy of the delivery systems, particularly in the case of small-scale production systems or those in remote and insecure areas, and the vaccine cold chain. In Central and West Africa, the relevant RECs (ECOWAS, CEMAC, CEBEVIRHA, WAEMU, etc.) and other regional organizations continue to strengthen their political commitment as well as their financial and technical support together with their development partners. National and regional control and eradication strategies are being prepared.

Disease situation and government policies by country

Tables 6 and 7 below have been completed with the information received from the questionnaires sent to the DG and DVS for PPR.

Table 6 covers the disease situation (if it is notifiable or not), the presence of official surveillance and/or control programs, and the treatment situation. Table 7 refers to the vaccination situation.

The definitions that were given to the respondents are:

> [1]Surveillance: is the systematic ongoing collection, collation and analysis of data and the timely dissemination of information to those who need to know so that action can be taken.
>
> [2]Control: a program which is approved, and managed or supervised by the Veterinary Authority of a country for the purpose of controlling a vector, pathogen or disease by specific measures applied throughout that country, or within a zone or compartment of that country.

Table 6: Official status, official programs and treatment for PPR in the countries of interest. Information provided by the questionnaire sent to the DG/DVS as part of this monograph. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

Country	Notifiable (yes/no)	Official surveillance[1] program (yes/no) (if yes, active or passive)	Official control[2] program (yes/no)	Treatment (Chemotherapy)	
				Treatment authorised (yes/no)	Frequently practiced (yes/no)
ASIA					
Bangladesh	Yes	Yes, passive	Yes (limited to some districts)	Yes	Yes
Myanmar (Burma)	Yes	Yes, passive	No	No	No
Nepal	Yes	Yes, active	Yes	N/A	N/A
Vietnam*	No	No	No	-	-
AFRICA					
Burkina Faso					
Côte d'Ivoire (Ivory Coast)	Yes	Yes, passive but active if outbreak	Yes	No	-
Kenya	Yes	Yes, passive	Control strategy in place	No	No
Malawi	Yes	Yes, active and passive	Yes	N/A	N/A
Mali	Yes	Yes, passive	Yes	No	No
Rwanda	Yes	Yes, active and passive	Yes	No	No
Tanzania	Yes	Yes, active and passive	Yes	No	No
Uganda	Yes	Yes	Yes	Yes	Yes
Zambia	Yes	Yes, active	Yes	Yes	No

* The reply from Vietnam is surprising but might have been a mistake with the line below (sheep and goat pox) in the questionnaire.

Table 7: Vaccination for PPR in the countries of interest. Information provided by the questionnaire sent to the DG/DVS as part of this monograph. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

Country	Vaccination			
	Compulsory vaccination (yes/no)	Who pays for the vaccine (Government, farmers, combination, others-specify)	Who delivers the vaccine (official, private vaccinators or both)	Species vaccinated (cattle, sheep, goats, pigs, poultry)
ASIA				
Bangladesh	No	Combination. Government subsidy, farmers pays a service charge	Government and private	Goat and sheep
Myanmar (Burma)	No	-	-	-
Nepal	No	Government	Official	Sheep and goats
Vietnam	No	-	-	-
AFRICA				
Côte d'Ivoire (Ivory Coast)	-	Government / Farmer	Government	Sheep and goats
Kenya	As per strategy	Combination	Both	Sheep and goats
Malawi	No	N/A	N/A	N/A
Mali	Yes	Combination	Official	Sheep and goats
Rwanda	Yes	Government	Official	Goats and sheep
Tanzania	Yes	Combination	Both	Goats and sheep
Uganda	No	Government	Both	Goats and sheep

Zambia*	Yes	Government	Official	Goats

*I t is surprising that Zambia vaccinates for PPR, as it only had a couple of outbreaks. Might be in the risk areas, but needs to be confirmed.

Vaccines Available

In the absence of homologous vaccines, and since Rinderpest virus (RPV) and PPRV share a high homoloogy at the nucleotide level, and a high degree of antingenic cross-reactivity, the attenuated tissue culture RPV vaccine was used for a long time as an heterologous vaccine, to protect small ruminants against PPR.

At the end of 1980s, the first homologus vaccine was developed when a PPRV strain was successfully attenuated by Diallo and colleagues [9]. It was based on a PPRV isolated by from Nigerian goats that had died from PPRV infection in 1975 (Nigeria 75/1) and was adapted to Vero cells at 37°C . The isolate was proved to be a powerful substitute for the heterologous vaccines.

In 1998, OIE endorsed the use of homologous vaccines in countries that had decided to follow the 'OIE pathway' for epidemiological surveillance for rinderpest, and after the global RP eradication, the OIE made clear that heterologous vaccines should not be used.

Live attenuated vaccines

The only currently available PPR vaccines, are cell culture-attenuated strains of natural PPRV. The first vaccine, the Nigeria 75/1 has been used extensively in Africa and the Middle East, but other strains have also been developed. Currently, there are six available PPR vaccine strains:

1. Nigeria 75/1 (Nigeria, lineage II; isolate of goat origin)
2. Sungri 96 (India, lineage IV; isolate of goat origin)
3. Arasur 87 (India, lineage IV; isolate of sheep origin)
4. Coimbatore 97 (India, lineage IV; isolate of goat origin)
5. Titu (Bangladesh, lineage IV; isolate of goat origin)
6. 45G37/35-K PPR Vaccine (Kazakhstan, lineage IV?).

DOSE: Studies with the Nigeria 75/1 calculated the effective dose to be $10^{0.8}$ $TCID_{50}$/animal; however, a dose of 10^3 $TCID_{50}$/animal also proved to be safe [10]. The OIE says that normally, the minimum immunising dose is 100x the lowest dose of vaccine virus able to induce 50% immunising response, and for Nigeria 75/1, the minimum titre is $10^{2.5}$ $TCID_{50}$.

ONSET OF IMMUNITY: After vaccination with standard PPRV vaccines, antibodies can be detected clearly at 14 days post vaccination. Full protection is achieved from standard doses of vaccine at three weeks post vaccination. Anti-PPRV antibodies elicited by the Nigeria 75/1 vaccine are highest during 30 to 45 days post-vaccination [11]. There are no studies investigating if protection can be achieved earlier with higher doses of vaccine.

EFFICACY and DURATION OF IMMUNITY: The vaccine in the field was shown to be protective against wild-type PPRV virus. With the Nigeria 75/1 prescribed vaccine dose of $10^{2.5}$ $TCID_{50}$, a single injection confers a long lasting immunity (at least 3 years) against all known PPRV genotypes (to date, a single serotype has been described), in all parts of the world in which it has so far been used (from Africa through to China).

SAFETY: A number of field trials were conducted on more than 98,000 sheep and goats in the period 1989–1996, demonstrating that the Nigeria 75/1 vaccine could not cause unwanted side effects such as abortion in pregnant animals, and vaccinated animals were unable to transmit the challenge virus to others [12]. Pregnant animals remained safe and were able to pass passive immunity to their offspring, which remained protected for 3–5 months. Reversion to virulence experiments were done with the Nigeria 75/1 strain. No reversion was observed after three back passages in animals. Importantly, after more than 25 years of use in field situations, including vaccination in PPR outbreaks, no incident has been noticed [1].

DIFFERENT STRAINS:

According to Sen et al, 2010 [12], since lineage IV is mostly restricted to Asian countries, the use of Nigeria 75/1 vaccine in Asian countries may increase the likelihood of mixing up of lineages and the development of mutants with high virulence. Thus, it is imperative to consider using the lineage-specific vaccine available for use in Asian countries. To this effect, some vaccines using lineage IV virus were developed in India (Sungri 96, Coimbatore 97 and Arasur 87). They all have been proven to be effective in terms of protection, and have been produced by passages in Vero cells. The Sungri 96 was the earliest vaccine strain developed at the Rinderpest Laboratory, Indian Veterinary Research Institute (IVRI) from an isolate from Sungri, in Himachal Pradesh. The genome sequence of Sungri 96 showed 96 to 99 % identity with the Asian isolates and 89 to 92 % identity with the African isolates. The Sungri 96 vaccine has been tested extensively in the laboratory and field to demonstrate that it was safe and efficacious in sheep and goats. It has also been demonstrated that it can provide sterile immunity for at least 6 years and therefore is used throughout India to vaccinate sheep and goats with great efficacy [12].

The Arasur 87 and Coimbatore 97 were originally isolated from southern part of India. Although the Arasur 87 is closely related to the Sungri 96 in antigenicity, both can easily be differentiated based on the pattern of cytopathic effect and the degree of neutralization using specific monoclonal antibodies [13].

In the study done by Saravanan et al., 2010 (14)[14], the potency of 4 of these vaccines was tested in accordance with OIE guidelines. The vaccines tested were the Sungri 96 produced by IVRI, Arasur 87 produced by TANUVAS (Tamil Nadu Vet Sciences University), Arasur 87 produced by IAH&VB (Institute of Animal Health and Veterinary Biologicals, Bangalore) and Coimbatore 97 produced by TANUVAS. There were 6 goats vaccinated with each vaccine, and 2-4 sheep vaccinated. The results showed that Sungri 96 and Arasur 87 (TANUVAS) protected sheep and goats from clinical signs, all swabs collected were negative for the virus and all animals were ELISA positive. Animals vaccinated with Coimbatore 97 were protected from clinical signs and all swabs were negative, but there was not 100% seroconversion. The vaccine Arasur 87 from IAH&VB did not protect goats from clinical signs (there was only one sheep protected, as the other one died of unrelated causes, so due to the small numbers it is not possible to conclude on sheep protection), the swabs were positive for PPRV, and animals did not show sero-conversion. The differences between the 2 strains of Arasur 87 were not ascertained.

No information has been found on the Titu strain from Bangladesh, besides their mention in several papers with no details.

As for the 45G37/35-K information has been found in Russian, and the below information has been obtained with Google translate; therefore caution is needed with its interpretation. The original link for the information is: **http://ej.kubagro.ru/2012/09/pdf/31.pdf**. In 1990, in the former USSR, a 45G37 vaccine was obtained using primary cell cultures of kidneys and testicles of sheep and goats, and later passaged in Saiga kidney cells at VNIIVViM (State Science Institution National Research Institute of Veterinary Virology and Microbiology of Russian Academy of Agricultural Sciences). High immune responses were induced 14-21 hours after vaccination.

It is possible that the original references is: A study of cultural properties of the vaccine strain 45G37 / 35-K virus peste des petits ruminants / IP Mikhalkin , TF Gorshkov, LI Anisimova et al. // Scientific basis for the production of veterinary biologicals. - Shchelkovo, 2005, pp 163-166.

http://www.dissercat.com/content/optimizatsiya-uslovii-kultivirovaniya-virusa-chumy-melkikh-zhvachnykh-dlya-polucheniya-diagn#ixzz40yOGsBUL

DIVA: The available PPR vaccines do not support the DIVA principle. The only vaccines in use are attenuated forms of the virus, and there is no consistent difference in antibody responses to these viruses and wild-type forms of the virus.

THERMOTOLERANCE: Although all the mentioned vaccines are highly efficacious, they are susceptible to thermodegradation, thereby requiring transportation at 2 to 8 °C and be stored at −20 °C. There are many publications and attempts to increase thermotolerance, from chemical stabilizers, to the use of thermo adapted strains. Many of them claim good results but the only one that has been independently validated to be used in a commercial process, and so far has commercially been used in Africa is the Xerovac technology as described by

Worrall et al, 2001 [15] in which viruses are dehydrated in vitro, within 18 h, in an excipient containing trehalose. With this process, the vaccine resisted 45°C for a period of 14 days with minimal loss of potency. However, the Xerovac is limited by technological conditions, and some African laboratories have ceased using it.

Chemical stabilizers

Different stabilizers, such as lactalbumin hydrolysate-sucrose (LS), Weybridge medium (WBM), lactalbumin hydrolysate-mannitol (LM), buffered gelatine-sorbitol (BUGS) and trehalose dihydrate (TD), have been evaluated to prepare lyophilized PPR vaccines. The OIE recommends the use of WBM as a chemical stabilizer for PPR lyophilized vaccines, but vaccines are still susceptible to thermal degradation in the absence of a cold-chain system. Asim et al. 2008 [16], reported that PPR vaccine lyophilized with the WBM was more stable and maintained the virus titre longer than with two other stabilizers. In contrast, another study conducted by Sarkar et al 2003 [17], revealed that the PPR vaccine lyophilized with either LS or TD is more stable than with both WBM and BUGS, having an expiry period of at least 45 days at 4 °C, 15– 19 days at 25 °C and 1–2 days at 37 °C. However, at 45 °C, BUGS had a marginal superiority, although lasted for few hours, followed by TD and LS with respect to shelf-life, LS and TD with respect to half-life. See Table 8.

Riyesh et al. 2011 [18] assessed two stabilisers, LS and stabilizer E (trehalose, $CaCl_2$ and $MgCl_2$) for their stability at different temperatures, using Thermo adapted strains developed in India. The results showed that both the stabilizers performed equally well with regard to shelf-life and half-life, and showed an expiry period of 24-26 days at 25°C, 7-8 days at 37°C and 3-4 days at 40°C. The LS was superior at 42 °C with a shelf-life of 44 h, whereas in stabilizer E, a 40 h shelf-life with a comparable half-life was observed. At 45 °C, the half-life in stabilizer E was better than in LS and lasted for 1 day. See Table 8. The vaccine in stabilizer E fared better in 1 mol/L MgSO4 diluent for 30 h at 4 °C and for 24 h at 25 °C as well as at 37 °C. The same vaccine with the LS, 1 mol/L MgSO4 was found suitable for 48 h at 4 °C but at 25 °C and 37 °C, the stability lasted for 24–30 h.

A publication from Silva et al 2011 [19] reported good results using a Tris/Trehalose formulation, compared to WBM. Data in Table 8 shows the data presented in the results section of the paper (which seems different from the abstract). Later on, this formulation was evaluated with good results by the same authors, with the vaccine produced at the National Veterinary Institute in Ethiopia, especially at 37 and 45°C. It is not clear the shelf and half-life obtained that time [20].

Mariner et al, presented data on thermostability of various formulations of PPR vaccines using lactalbumen hydrolysate (LAH) 2.5% with 5% sucrose, or with 5% trehalose. They also used 5% trehalose alone and Xerovac. The results have not been published in a peer-reviewed journal, and are only available in the **Proceedings of the Global PPR Alliance Meeting**, April 2013, pages 29-30. The results are difficult to interpret, there is no clarity on results and groups, and there seem to be inconsistencies between statements in the abstract and the body of the poster presentation. It is difficult to judge these formulations without the detailed information. It was not possible to include the data in Table 8.

Siddique et al 2006 [21] used a thermostable vaccine produced in Bangladesh, and confirmed its efficacy in goats after keeping the vaccine at room temperature (25-30°C) for 14 days. The methodology used for the vaccine is the one described in: Chowdhury SMZH, Shukur A, Nasiruddin M, Ara MR, Ferdous KS, Sobhan Z, Habib S, Das BK and Litamoi JK (2004). Molecular characterization of PPR virus: Experiential development of PPR thermostable vaccine. Annual Research Review Workshop-2004, Bangladesh Livestock Research Institute, Savar, Dhaka, 9-10 May 2004. It has not been possible to find that reference, but being Dr Litamoi the last author, it is quite safe to assume that it is based on the Xerovac technology.

In Nigeria, El-Yuguda et al 2014 [22] did a field evaluation of a thermostable vaccine produced with a variation of the Xerovac technology. The vaccine elicited protective immune response in vaccinated goats and vaccinated animals resisted challenge to experimental infection with virulent PPR virus. The vaccine maintained good titres at room temperature for 8 hours, but dropped after 15 hours. They also evaluated different routes, and concluded that the vaccine could also be given orally.

Thermo-stable vaccine strains

Another method to improve thermostability of PPR vaccines is the use of thermo-stable vaccine strains in terms of their stability at ambient temperature. In order to achieve intrinsic thermo-resistance in a virus, the native virus can be grown successively for many passages at higher temperatures and it may result in an intrinsically thermo-resistant virus clonal population. Such an adapted thermo-resistant virus clonal population can be then grown at a higher temperature than the usual temperature of 37°C, in thermo-adapted (Ta) cell lines. In this approach, the results are largely empirical as they depend on the capability of the virus to resist detrimental effect of high temperature. Selection and subsequent propagation of the virus clonal population, their stability, and maintenance of their immunogenic potential need to be assessed before considered them as a vaccine candidate [23].

IVRI in India, have developed two thermostable vaccines: Revati and Jhansi [12], and tested their thermal degradation profile. At 37 and 40°C, these thermostable vaccines had a shelf life of 7.62 and 3.68 days, respectively, when compared with 1.58 days at 37°C for native Sungri/96 vaccine. The novel thermostable vaccines developed were also tested after reconstitution. Different stabilizers were evaluated for these strains (see Table 8 and previous comments on stabilizer E). More details are available for the Jhansi strain, published by Balmurugan et al, 2014 [23]: The lineage IV virus was attenuated up to 50 passages in Ta Vero cells, at which, the virus was found sterile, innocuous in mice and guinea pigs and safe in seronegative goats and sheep. The developed vaccine was tested for its immunogenicity in goats and sheep by SC inoculation of 100 TCID50 (0.1 field dose), 103 TCID50 (one field dose) and 105 TCID50 (100 field doses) of the attenuated virus along with controls as per OIE described protocols.

Table 8: Comparison of shelf-life (SL) and half-life (HL) of different strains of PPR vaccine, using different stabilisers at different temperatures. Source: Modified from Liu et al, 2014 [13], incorporating data from Silva et al, 2011 [19].

References		Sarkar et al, 2003					Riyesh et al, 2011				Silva et al, 2011			
Stabilizers		LS	WBM	BUGS	2.5 % TD	5 % TD	LS	LS	E	E	WBM (L)	Tris/Tre (L)	WBM (Ly)	Tris/Treh (Ly)
Strain		Sungri 96	Sungri 96	Sungri 96	Sungri 96	Sungri 96	Jhansi 2003	Revati 2006	Jhansi 2003	Revati 2006	Nig 75/1	Nig 75/1	Nig 75/1	Nig 75/1
SL	4°C	ND	123 d	239 d	2051 d	ND	ND	ND	ND	ND				
HL		ND	30 d	42.25 d	500 d	ND	ND	ND	ND	ND	22 d	30 d	11 m	10 m
SL	25°C	15 d	5 d	12 d	16 d	19 d	23.29 d	22.28 d	25.64 d	22.56 d				
HL		4.76 d	1.83 d	2.17 d	4.67 d	4 d	4.68 d	4.9 d	4.62 d	4.81 d				
SL	37°C	1.58 d	ND	1.55 d	1.05 d	1.96 d	7.62 d	6.82 d	6.95 d	5.51 d				
HL		17.8 h	10 h	7.79 h	8.57 d	14.07 h	1.76 d	2 d	1.94 d	1.8 d	9 h	21 h	7 h	67 h
SL	40°C	ND	ND	ND	ND	ND	3.68 d	2.61 d	3.48 d	2.29 d				
HL		ND	ND	ND	ND	ND	0.66 d	0.59 d	0.72 d	0.67 d				
SL	42°C	ND	ND	ND	ND	ND	43.18 h	23.8 h	39.25 h	40.5 h				
HL		ND	ND	ND	ND	ND	10.6 h	7.12 h	11.1 h	9.68 h				
SL	45°C	5.72 h	0.56 h	10.8 h	7 h	8.11 h	22.87 h	9.52 h	24.67 h	26.95 h				
HL		2.29 h	1.33 h	2.4 h	1.3 h	1.96 h	6.21 h	4.14 h	8.4 h	12.87 h			-	49 h

LS: Lactalbumin hydrolysate-sucrose; WBM: Weybridge medium; BUGS: buffered gelatin-sorbitol; TD: trehalose dehydrate; E: trehalose, CaCl2 and MgCl2; Tris/Tre: Tris–HCl, EDTA, Tween 80, Trehalose; L: Liquid; Ly: Lyophilized. ND: not done.

Strains: Jhansi 2003 and Revati 2006 are thermos-adapted strains.

NOTE: Attempts to include data from other sources mentioned in the monograph was made, but it was not possible due to the data not being presented in a comparable way.

Animals were assessed for PPRV-specific antibodies 7–28 days post vaccination (dpv) by PPR competitive ELISA and serum neutralization tests. The PPRV antibodies were detected in all immunized goats and sheep. The goats were challenged with virulent PPRV at 28th dpv (not the sheep), and they were protected. The attenuated vaccine did not induce any adverse reaction and provided complete protection even at low dose in goats when challenged with virulent virus. There was no shedding and horizontal transmission of the attenuated virus to in-contact controls. The results indicate that the developed PPR Ta attenuated virus is innocuous, safe, immunogenic and potent or efficacious vaccine candidate alternative to the existing vaccines for the protection. The paper does not present data on reversion to virulence, but mentions a lack of apparent clinical signs and no shedding of the virus in the secretion of goats and sheep during the 3 needle passages indicating that the virus has been stably attenuated and the possible reversion to virulence is unlikely. However, it would be good to see the data. Dr Singh, IVRI Director, was contacted for an update on the status of this candidate. He said they are doing some additional validation trials, and they are expecting to have the product ready in one year.

Inactivated vaccines

Killed vaccines are not available and, owing to the immunological response to PPRV, would not be fully effective. This may also be the reason why no experiments for the development of PPR killed vaccines and for testing their protection have been done. The experience of rinderpest eradication showed that killed rinderpest preparations (e.g. heated blood or other body fluids from infected animals) were ineffective at giving protection. Additionally, some data about the measles vaccines show that the inactivated measles vaccines, besides giving only transient protection, could lead to increased virulence of subsequent infection (atypical disease in about 20 % of cases), which is one of the reasons why killed measles vaccines are not used [1].

Main vaccine needs:

Current vaccines are very good, and similar vaccines were used for the eradication of Rinderpest. However, it would be beneficial to have vaccines that are/have:

1- Thermostable – this will make logistics of deployment easy

2- DIVA capabilities – will reduce the costs of the global eradication, especially (in regard to surveillance) at the end.

Commercial vaccines manufactured in Africa and Asia

The information summarized in Table 9 below, is based on information from The Center for Food Security and Public health, Iowa State University (www.cfsph.iastate.edu/vaccines/index.php and Vetvac (www.vetvac.org). African manufacturers that were not included in any of the databases have been included: Morocco, Cameroon and Kenya. More details have not been gathered, as another consultant has been commissioned to perform this task.

Table 9: Manufacturers of PPR vaccines in Asia and Africa.

Manufacturer	Country	Name	Strain	Countries distribution
ASIA				
Tiankang Biopharmacuetical	China	Peste des Petits Ruminant		China
Hester Biosciences Limited	India	PPR Vaccine	Sungri 96 strain	India
	Nepal	PPR Vaccine	Nigeria 75/1	
Indian Immunologicals Limited	India	Raksha PPR	Sungri 96	India
Institute of Animal Health and Veterinary Biologicals [Karnataka]	India			India
MSD Animal Health (Merck)		Ovilis PPR	Sungri '96	India, Kuwait
AFRICA				
Botswana Vaccine Institute	Botswana	PPR-VAC®	Nigeria 75/1 (EMVT)	Botswana, Iran, UAE.
LANAVET	Cameroon	Capripestovax	Nigeria 75/1	Cameroon
National Veterinary Institute of Ethiopia	Ethiopia	PPR	75/1/LK 6Vero76	Ethiopia
Veterinary Serum and Vaccine Research Institute	Egypt	PPR-TC Vaccine Attenuated	Nigeria 75/1	Egypt
Kenyan Veterinary Vaccines Production Institute	Kenya	Pestevax	Nigeria 75/1	

MCI Sante Animale	Morocco	Ovipox	Nigeria 75/1	
	Morocco	Lyopox	PPR combined with Sheep & goat pox	
National Veterinary Research Institute	Nigeria	Peste des Petits Ruminants Virus Vaccine	Nigeria 75/1	Nigeria
Institut Sénégalais de Recherches Agricoles [ISRA]	Senegal	PPR	Nigeria 75/1	Senegal
Veterinary Research Institute [Central Veterinary Research Laboratories]	Sudan	PPR	Nigeria 75/1	Sudan

Additionally, PPR vaccines are produced in Turkey, Jordan and Pakistan.

Commercial vaccines imported into Africa and Asia

The information summarized in Table 10 is based on the questionnaire sent to the Directors of Veterinary Services office and regulators of the countries of interest. For a list of respondents, please see Annex 2. Note that some vaccines might have been imported under DVS dispensation, and they are not necessary licensed in the country.

Table 10: Commercial PPR vaccines imported into the countries of interest. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa. (Note: The disease has never been reported in Madagascar, Malawi, Mozambique and South Africa, therefore no vaccination is expected.)

Country	Vaccine name	Strain or type	Country of origin	Doses imported 2015	Doses imported 2014	Doses imported 2013	Doses imported 2012
ASIA							
Bangladesh	N/A	-	-	-	-	-	-
Myanmar (Burma)	-	-	-	-	-	-	-
Nepal	-	-	-	-	-	-	-

Vietnam	-	-	-	-	-	-	-
AFRICA							
Côte d'Ivoire (Ivory Coast)	Capripestovax*	Nigeria 75/1	Ethiopia	400,000	80,000	-	-
Kenya	-	-	-	-	-	-	-
Malawi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mali	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Rwanda	-	-	-	-	-	-	-
Tanzania**	Pestevac	Nigeria 75/1	Jordan		1,000,000	3,000,000	4,225,000
Uganda***	Lyopox	Nigeria 75/1 + SGP	Morocco	1,000,000			
Uganda****		Nigeria 75/1	Kenya			100,000	
Zambia	-	-	-	N/A	N/A	N/A	-

- Questionnaire received, no information provided.

*: That is the name of the vaccine produced in Cameroon, and not in Ethiopia, so there must be some confusion. However, both are based on the Nigeria 75/1 strain.

**: Information provided by the DVS office. The questionnaire received from the Regulatory Authorities, does not mention any PPR imported vaccines.

***: Information provided by the DVS Office. They also commented that in 2011, they imported 1,558,500 PPR doses from Egypt

****: Information provided by the regulatory authorities

Other comments: JOVAC, the manufacturer from Jordan was also sent a questionnaire designed for key importers into the region. They confirmed that they export PPR vaccine to Africa and Asia. They did not specify the countries or the volumes.

Combination vaccines

- Current use: Currently, the only commercial combination vaccine, is the one produced by MCI Sante Animale in Morocco, called Lyopox PPR. It is a combination vaccine (not a recombinant product), using PPR (strain Nigeria 75/1) and Sheep pox (Romania strain).
- **http://www.mci-santeanimale.com/media/produit/pdf/en/prden402590-ang-lyopox-ppr-pdf.pdf**
- Desirable combinations: PPR, CCPP, SGP, RVF but variable depending on the diseases present in the area.

Characteristics of Ideal Vaccine Candidates for Smallholders

The Target Product Profiles (TPPs) reflect the availability and utility of current agents and incorporate features that will be necessary to improve on the current products and to address unmet needs, taking into account the particular requirements of the poorest livestock keepers.

The TPPs are more robust when they include the opinions and consider the needs of the different stakeholders. While efforts have been made to encompass them, the TPP showed in Table 11 below, should be considered a proposal, a live document subject to improvements.

Information on current vaccines has been obtained from the datasheet of different products as per links below:

Ovivax PPR (MCI Sante Animale, Morocco):

http://www.mci-santeanimale.com/media/produit/pdf/en/prden413237-ang-ovivax-ppr-pdf.pdf

PPR-VAC™ (BVI, Botswana): **http://www.bvibw.com/common_up/bvi-new/files/PPR%20-%20VAC.pdf**

PPR Vaccine (Hester, India – Sungri 96 strain): **http://www.hesterbiosciences.co.in/ppr-vaccine.php**

Pestevac® (Jovac, Jordan):

http://www.jovaccenter.com/userfiles/file/9-06-2014/Large%20Animals%20Vaccines%20/Pestevac-En.pdf

Table 11: Target Product Profile (TPP) PPR vaccine – Proposal:

	Attribute	Minimum (current available vaccine)	Ideal
1	Antigen	Immunogen with protective antigens against field/wild-type PPRV	Immunogen with protective antigens against field/wild-type PPRV
2	Indication for use	For active immunization of goat & sheep to prevent incidence of PPR	For active immunization of goat & sheep to prevent infection of PPR
3	Recommended species	Goat & sheep	Goat & Sheep
4	Recommended dose	OIE: 100x the lowest dose able to induce a 50% immunising response. For Nigeria 75/1 strain the required minimum titre is $10^{2.5}$ $TCID_{50}$ Volume: 0,5 ml – 1 ml depending on manufacturer	1 ml
5	Pharmaceutical form	Freeze dried	Thermostable at high ambient temperatures akin to those demonstrated with Xerovac
6	Route of administration	SC (behind the elbow) Other manufacturers recommend at mid neck or thigh region.	SC or IM
7	Regimen - primary vaccination	One dose Hester (India) recommends to vaccinate after lambing season or during onset of breeding season.	One dose
8	Regimen - booster	Annual injection is recommended	Lifelong immunity after primary vaccination
9	Epidemiological relevance	The 6 PPR vaccine strains appear to cross-protect against various global PPRVs	Single vaccine for global use
10	Recommended age at first vaccination	• One dose at 2 months of age, for animals from unvaccinated mothers. One dose at 4 months	1 month of age

		of age from vaccinated mothers. • Another manufacturer says one dose for animals over 6 months, and two doses at 2-6 month interval for animals under 6 months. Other manufacturer says vaccinate at 2-3 months of age, and revaccinate after 4 months.	
11	Onset of immunity	3 weeks post vaccination	One week following vaccination
12	Duration of immunity	3 -5 years, practically lifelong	Lifelong
13	Expected efficacy	To prevent disease & prevent mortality >90% animals	To prevent infection and transmission in 100% of the animals.
14	Expected safety	No abortions in pregnant animals; no transmission of vaccine virus to others; passive immunity to offspring for at least 3 months; no recorded reversion to virulence	No local or systemic post-vaccination reactions plus all noted for currently used PPR vaccines in the left column
15	Withdrawal period	Zero days	Nil
16	Special requirements for animals	Only vaccinate healthy animals. - Because of the particular sensitivity of the pregnant goats to injections, it is not recommended to vaccinate them, except in emergencies.	Vaccinate all animals
17	Special requirements for persons	None	None
18	Package size	50 - 100 doses	Multiple pack size from 10 doses
19	Price to end user		

20	Storage condition and shelf-life as packaged for sale	Store between 2 to 8 °C. Stable for 2 years.	≥ 24 months 4-8° C and/or 48 hours at 30°C
21	In-use stability	Use reconstituted vaccine immediately. Some manufacturers say should not be used more than 2 hours after reconstitution.	Use reconstituted vaccine up to 48 hours & beyond
22	Other	All inoculation equipment should be cleaned with water only and sterilized in boiling water. Antiseptics should not be used. Molar solution of magnesium sulphate or a buffered physiological saline should be used as the solvent	

Limitations

Scientific quality: The publications and data from the different research groups, should be carefully evaluated. The use of good science and good experimental design with use of proper controls, adequate numbers, suitable challenge model, reproduction of results by them and by independent groups, and appropriate analysis has not been verified for this monograph. If any of these projects were to be pursued, a detailed peer review taking into account the above considerations is strongly recommended.

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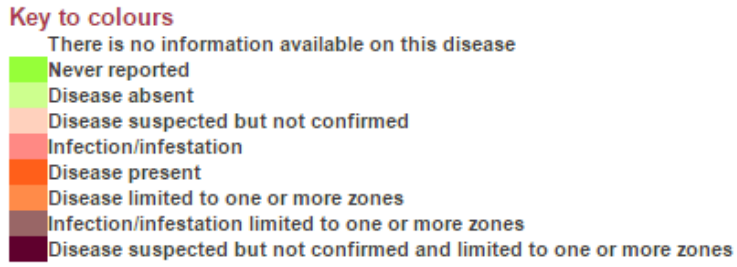
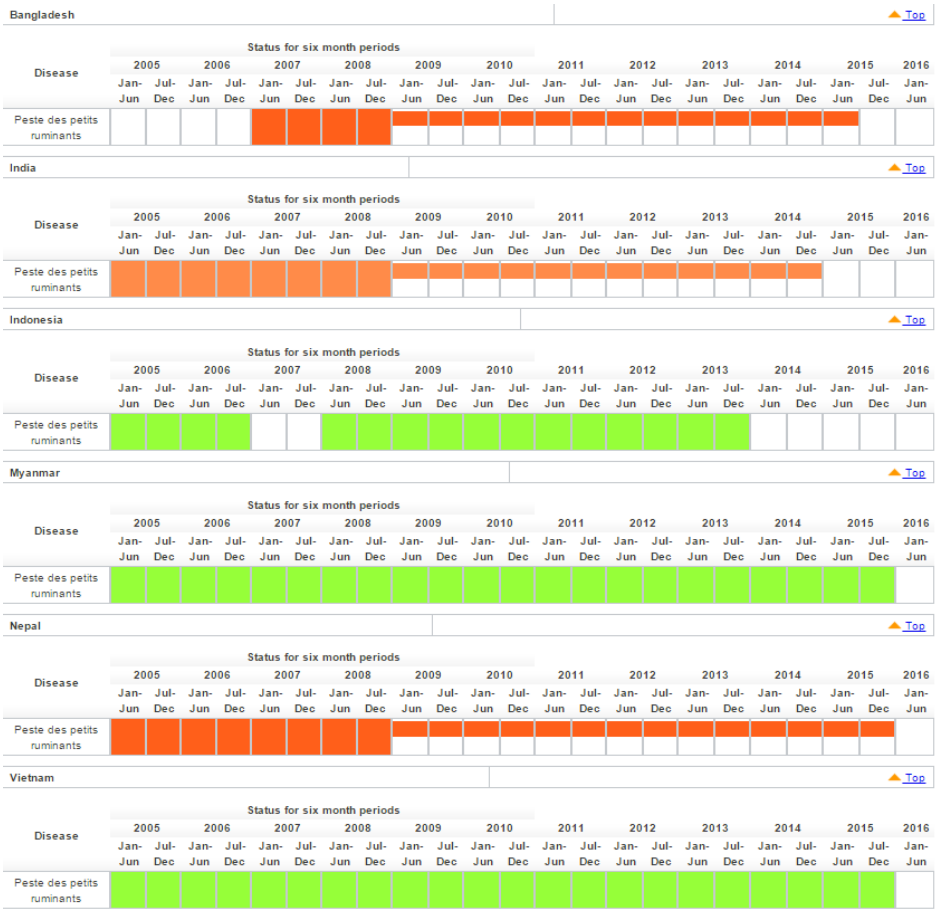
Annex 1: Additional data on disease presence and incidence

Reports to OIE on PPR:

When different animal health statuses between domestic and wild animal population are provided, the box is split in two: the upper part for domestic animals, and the lower part for wild animals.



PPR in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam

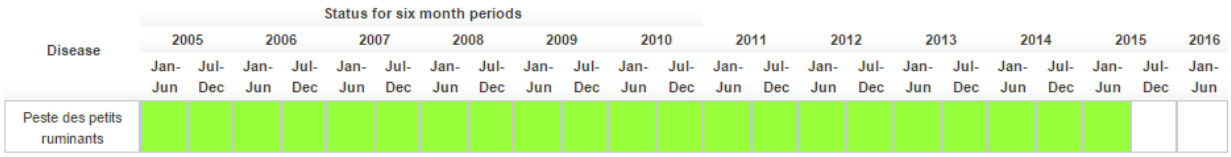


PPR in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal

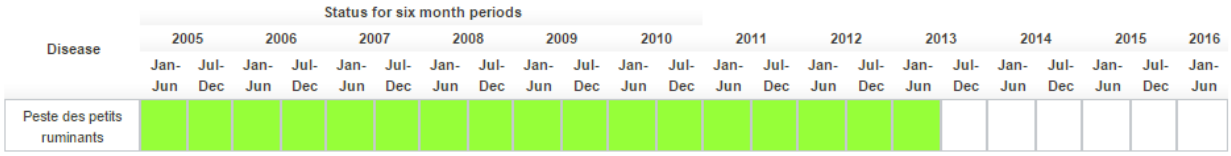
PPR in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda

PPR in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia

Madagascar Top



Malawi Top



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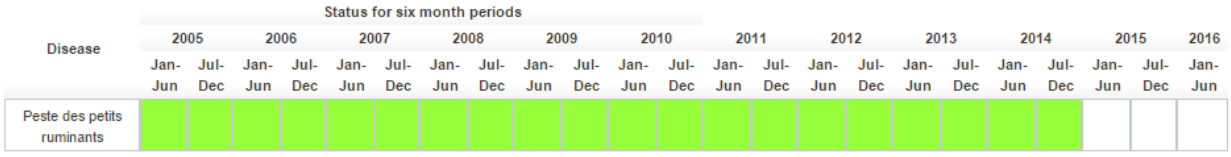
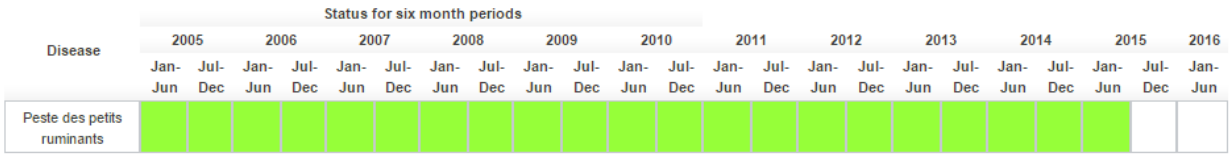


South Africa Top



Zambia Top